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EXAMINER	
HIRIYANNA, KELAGINAMANE T	
ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,455	VAN DER BURG ET AL.	
	Examiner	Art Unit	
	KELAGINAMANE HIRIYANNA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-12 and 26-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 7-12 and 26-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on *03/12/2010* in response to office action mailed on 06/22/2009 has been acknowledged.

Claims 1, 7-8, and 11 are amended.

Claims 2-6 are canceled.

Claims 26-41 are new.

Claims 1, 7-12 and 26-41 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

Withdrawn: Claim 1 and 4 rejection as failing to define the invention in the manner required by 35 U.S.C. 112, second paragraph for the reasons of record as set forth in the office action mailed on 06/22/2009 is withdrawn in view of Applicants amendments and cancellation to claims in the response of *03/12/2010*.

Withdrawn: Claims 1-2 and 4-5, rejection under 102(e) as being anticipated by Stuelpnagel et al., (US2005/0158702 A1) for the reasons of record as set forth in the office action mailed on 06/22/2009 is withdrawn in view of Applicants amendments and cancellation to claims in the response of *03/12/2010*.

Withdrawn: Claims 1-2 and 4-5, rejection under 102(b) as being anticipated by Walt et al., (US 6210910B1) for the reasons of record as set forth in the office action mailed on 06/22/2009 is withdrawn in view of Applicants amendments and cancellation to claims in the response of *03/12/2010*.

Withdrawn: Claims 1-2, 4-5 and 11-12 rejection under 102(e) as being anticipated by Giuliano et al., (US 2003/0096322 A1) for the reasons of record as set forth in the office action mailed on 06/22/2009 is withdrawn in view of Applicants amendments and cancellation to claims in the response of *03/12/2010*.

Withdrawn: Claims rejections under 35 USC 103 (a) for the reasons of record as set forth in the office action mailed on 06/22/2009 is withdrawn in view of Applicants

amendments and cancellation to claims in the response of *03/12/2010* and further in view of a new rejection below.

.Withdrawn: Double patenting warning for the reasons of record as set forth in the office action mailed on 06/22/2009 is withdrawn in view of Applicants amendments and cancellation to claims in the response of *03/12/2010*.

Claim Objections

Claim 1 is objected to as it recites on line 5 "each cell line comprises a reporter", this is just not proper language. It should be either "wherein each cell line comprises a reporter" or "each cell line comprising a reporter".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim1 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are in claim recitation on line 6 "which is induced by a steroid ligand" and "a different steroid or thyroid hormone receptor", there is no linkage here. Is the steroid receptor required to be activated by the steroid ligand or not? If not, why is it there? Applicant is required to make appropriate correction to the same.

Claim1 rejected under 35 U.S.C. 112, second paragraph for lack of clarity as it recites on line 6 "each cell line comprises an expression plasmid coding for a different steroid or thyroid receptor; or a ligand modifying factor", how would a plasmid coding for a ligand-modifying factor work? If there is no receptor to respond to the ligand, It would not

activate the reporter. Hence, the claim is rejected for lack of clarity. The Applicant is required to clarify the same.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite as it recites in claim 1 on line 8 " a ligand modifying factor". The artisan would not know what ligand the applicant is referring to. Is it the steroid ligand or any ligand of a receptor in a cell. Applicant is required to clarify and make appropriate changes.

Claim 36 recites the limitation "the specific component" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 37 recites the limitation "the specific component" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 38 recites the limitation "the specific component" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Double Patenting Warning

Applicant is advised that should claim 1 be found allowable, claim 35 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 35 requires the ligand modifying factor be an enzyme, however, such depends from Claim 1, which requires the ligand modifying factor which is known in the art to be always an enzyme. Therefore, despite a slight difference in wording, Claim 35 is a substantial duplicate of Claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims *1, 7-12 and 26-41* are rejected under 35 USC 103 (a) as being unpatentable over Evans et al., (US patent No.:5,298,429) and Quaedackers et al et al (2001, Endocrinology 142:1156-1166; art of record) in view of Stuelpnagel et al., (US2005/0158702 A1; art of record), Walt et al., (US 6210910B1; art of record) and Wilson et al et al (2002, Toxicological Sciences 66:69-81; art of record).

The above claims are drawn to a method for determining the presence of one or more specific ligands in a sample comprising steps of contacting the sample with an array of cell lines comprising a reporter gene construct respnding a cellular pathway induced by different specific ligands, measuring the activity of reporter gene and determining by comparison the ligands in the sample.

Evans teaches bioassay for identifying ligands for steroid hormone receptors using recombinant cell lines expressing various hormone receptors and a DNA sequence encoding a hormone response element operatively linked to a reporter gene reporter gene (entire article; abstract). Evans further teaches recombinant cells for multiple steroid hormone receptors and their corresponding receptor constructs expressed in various cell lines (entire article; col. 87-90). Evans however, does not teach specifically using U2-OS cell lines for bioassays of steroid ligands or ligand modifiers.

Quaedackers teaches the limitation of using U2-OS cell line for expressing the hormone receptors and reporter gene assays for detecting the steroid ligands in samples (entire article; abstract). Quaedackers specifically teach plasmids expressing specific hormone receptors under the control of hormone responsive elements present in 3 random repeats upstream of the minimal adenovirus E1B TATA promoter sequence of SEQ ID NO:2 in pGL3 plasmid and hormone receptors is introduced in the PSG5 expression plasmid in osteoblastic U2-OS cell lines that could be used as an effective cell based detection or assay of several steroid hormones (entire article; abstract).

Evans and Quuaedakers however do not teach making biosesnsor cell arrays for detecting steroid ligands in a sample.

Regarding the limitation of cell arrays in claims Stuelpnagel teaches a biosensor array of one or more cells or cell lines and relies on the fact that individual cells which are biologically or chemically stimulated by the ligands in the cell environment and respond by

producing a change in the cell or cellular environment wherein said cell may comprise genetically engineered cells that are prokaryotic or eukaryotic, mammalian, primate etc and cell lines of any type for example osteoblast cells or chondrocytes etc (entire article; abstract; paragraphs 0030, 033-036, 0057-058). In general the cells are transformed using variety of vectors and constructs and used for functional assay of various analytes including biomolecules such as steroids etc (paragraphs 0096-0099) and in one embodiment the cell plasmids regulates the expression of marker or reporter genes such as luciferase or encoded GFPs (paragraphs 0111-0113) depending on the ligands or their concentrations in the sample.

Similarly Walt teaches a biosensor array of individual cells or randomly mixed population of cells having unique response characterstic to or chemical or biological materials or target analytes in the cell environment and respond by producing a change in the cell or cellular environment in a detectable manner (entire article; abstract; col.5, lines 55-68 briding col.6-9). Said cells of biosensor may comprise genetically engineered cells that are prokaryotic or eukaryotic, mammalian, primate etc and cell lines of any type for example osteoblast cells or chondrocytes etc (entire article; col.9, lines 35-54). In an embodiment the cells are transformed using variety of vectors and constructs and used for functional assay of various analytes including biomolecules such as steroids etc (co.l27) and regulate the expression of marker or reporter genes such as luciferase or encoded GFPs (col.15, lines 15-42; col.28) depending on the ligands or their concentrations in the sample.

Wilson teaches the limitation of plasmids expressing specific hormone receptors and deriving a cell line that could be used as an effective cell based biosensor for detecting several steroid hormones and for screening androgen agonists and antagonists etc. wherein cells could be arrayed in 96 well plates and effectively used for screening hormonally active chemicals (entire article; abstract).

Thus it would have been obvious for one of ordinary skill in the art to substitute the generic cell lines for harboring the several different steroid detection constructs taught by Evans with U2-OS cells taught by Quaedaker and further array said recombinant U2-OS cells in the form of biosensor arrays for detecting steroid ligands and ligand modifiers as

taught in Stuelpnagel, Walt or Wilson and generate live U2-OS cell based biosensor arrays for effectively detecting steroid hormones or their analogues in a sample or in the environment. One of ordinary skill in the art would have been motivated to make and use U2-Os cell arrays with hormone and related compound detection as they are more sensitive and effective in detecting said ligands in cellular environments. One of ordinary skill in the art would have reasonable expectation of success making and using biosensor of U2-OS cell arrays for detecting steroid receptor ligands and their modifiers because the art teaches that it is routine to make recombinant cells with specific receptor and reporter for detecting ligands, toxic chemicals that affect cell pathways and specifically steroid hormones. Thus, the claimed invention was *prima facie* obvious.

Conclusion:

No claim allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna Ph.D.,* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Thursday from 9 AM-7PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.,* may be reached at **(571) 272-0739.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-

direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

/Robert M Kelly/

Primary Examiner, Art Unit 1633